

# **Pertussis: Whoop (there it is!)**

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# Case #1

- 23-day old girl with 4-days of congestion, fever, cough and difficulty breathing
    - WBC 36.6 (S10, B8, L67)
    - CXR normal
    - NP DFA positive for Influenza A
  - Treated with amp/cefotax/cont albuterol
  - Developed worsening respiratory distress, with apnea and bradycardia, necessitating intubation, HFOV & then ECMO
  - Expired on hospital day #3
- 



## Case #2

- 2-month old boy with congestion and paroxysmal cough
  - ⊙ WBC 65.1 (N20, B4, L67, M7, E2)
  - ⊙ CXR: bilateral lower lobe infiltrates
- Treated with ceftriaxone and erythromycin
- Admission NP DFA and culture for pertussis were negative
- Gradual clinical improvement initially, but on HD #14, developed increasing tachypnea and paroxysmal coughing with O2 desats

## Case #3

- 3-year old with fever to 103.5F, paroxysmal cough and inspiratory whoop at least once per hour and worsening when supine
  - ⊙ WBC 22.8 (67S, 18B, 13L, 2M)
  - ⊙ CXR: RML infiltrate
  - ⊙ Pertussis titers: PT IgM 1 (<5); FHA IgM 48 (<20)
- Illness for 4 months, with “bronchiolitis” and “pneumonia” x 3 episodes, refractory to albuterol and antibiotics (incl. erythromycin)
- Treated with cefuroxime and erythromycin but no clinical improvement



# Pertussis




- Pertussis = Latin “intense cough”
- BaiReKe = Chinese “100 day cough”
- Translation: an intense cough that lasts a long time



# The Pathogen:

## *Bordetella pertussis*

- Fastidious tiny gram negative coccobacillus
  - Several virulence factors promote attachment and damage to the respiratory epithelium
    - ⊙ PT=Pertussis toxin (specific to *B. pertussis*): major virulence protein and promotes lymphocytosis
    - ⊙ FHA=filamentous hemagglutinin, PRN=pertactin, & FIM=fimbrial agglutinogens (less specific)
  - Transmitted person-to-person via large respiratory droplets (highly contagious)
  - Cyclical pattern with peaks every 3-5 years
- 






# Related Pathogen: *B. parapertussis*

- Incidence may be under-recognized
- Course generally, but not always, less severe than *B. pertussis*
  - ⊙ Does not produce pertussis toxin
  - ⊙ Not associated with seizures or encephalopathy
- No protection from pertussis vaccination

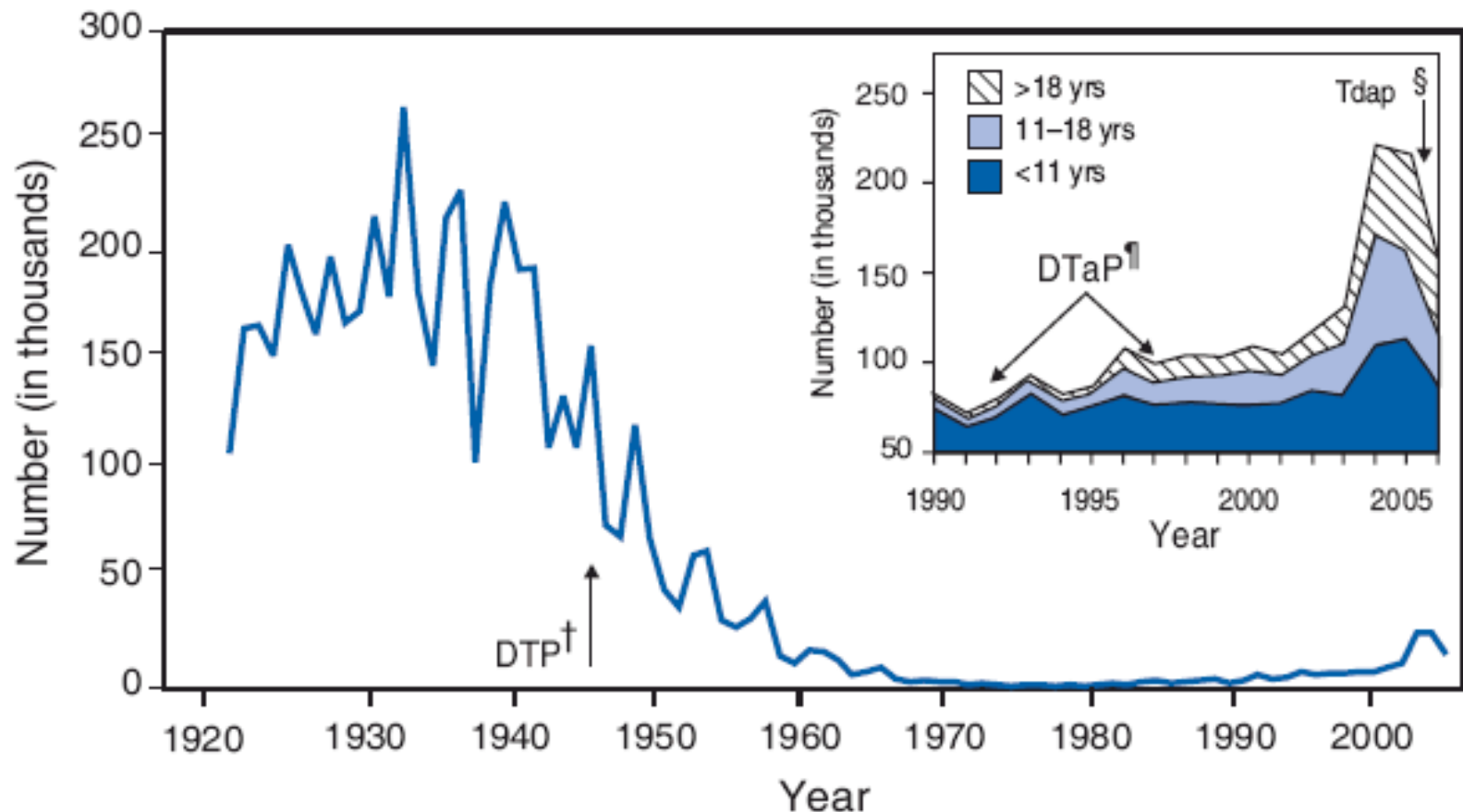


# Historical Perspective

- Pre-vaccine era (early 1900's - 1940's)
    - ⊙ 5 out of every 1000 live-born infants died from pertussis
    - ⊙ Leading cause of death from communicable disease in age <14 years in the US
    - ⊙ Peak in 1934 with 260,000 cases reported
  - Vaccine era (1940's - present)
    - ⊙ Dramatic decrease in reported incidence
    - ⊙ Mortality dropped 80 fold between 1944-1979
    - ⊙ Incidence has been increasing since 1990's
- 



# Reported Pertussis in U.S. (1922-2006)





# Age Shift in Pertussis Cases

- Largest increase in reported cases among those  $\geq 10$  yo
  - ⦿ 1978-1981: 12%
  - ⦿ 2001-2003: 56%
- Adolescents and adults are important reservoirs of infection for young infants





# Reasons for rising incidence...

- Waning of vaccine- and infection-induced immunity (waning after 5-10 years)
- Increased recognition and reporting
- Availability of better diagnostic tests
- ?Use of less potent pertussis vaccines
- ?Emergence of vaccine-resistant strains

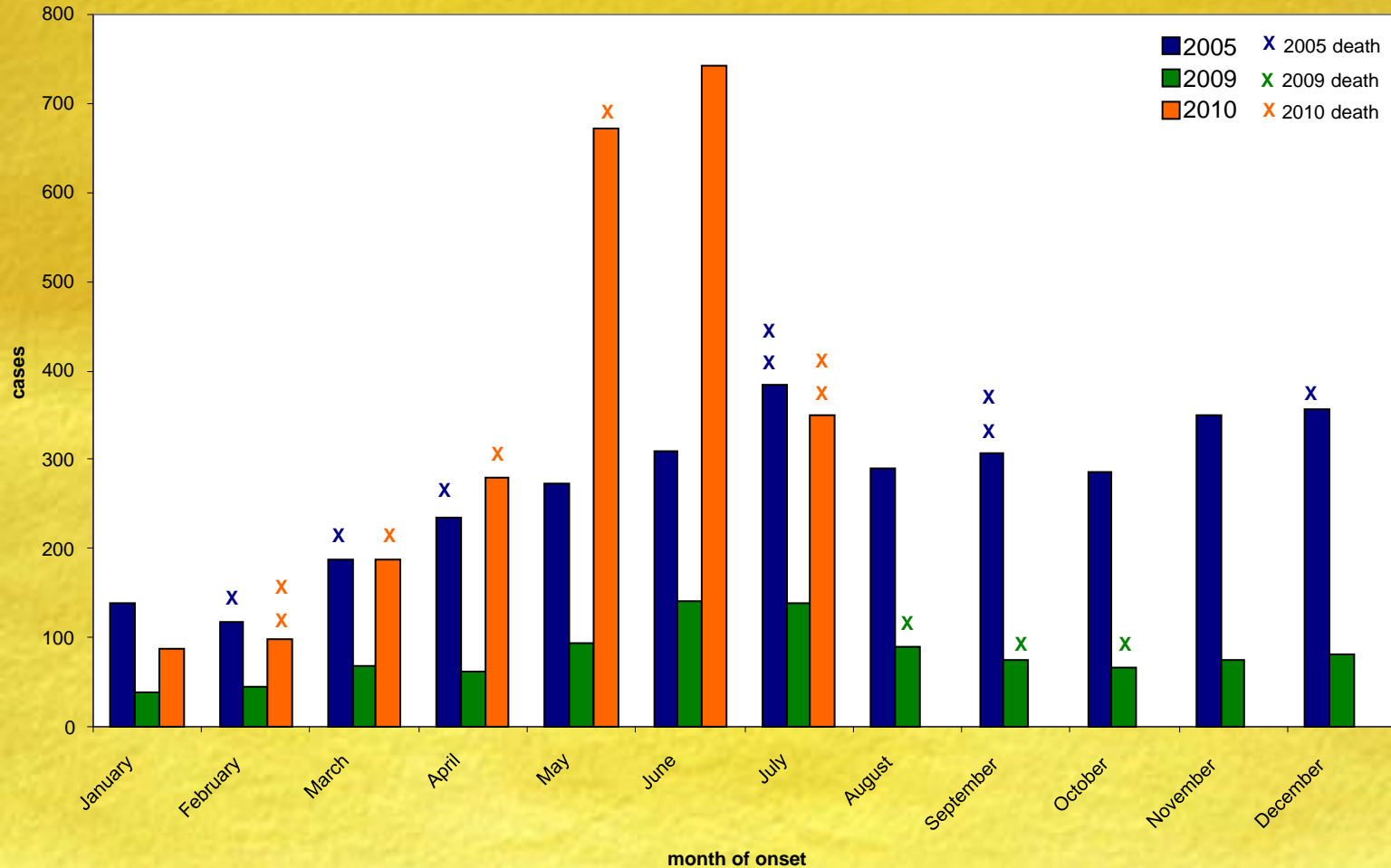


# Pertussis Epidemic California, 2010

- As of 8/10/2010, **2,774** cases of pertussis have been reported in CA (**7.0 cases/100,000**), a **7-fold increase** from the same time period in 2009 when **395** cases were reported
- If current trend continues, CA will see more cases of pertussis than it has in over 50 years
- Other states are reporting 2010 increases to CDC, but none are reporting increases similar to those in California

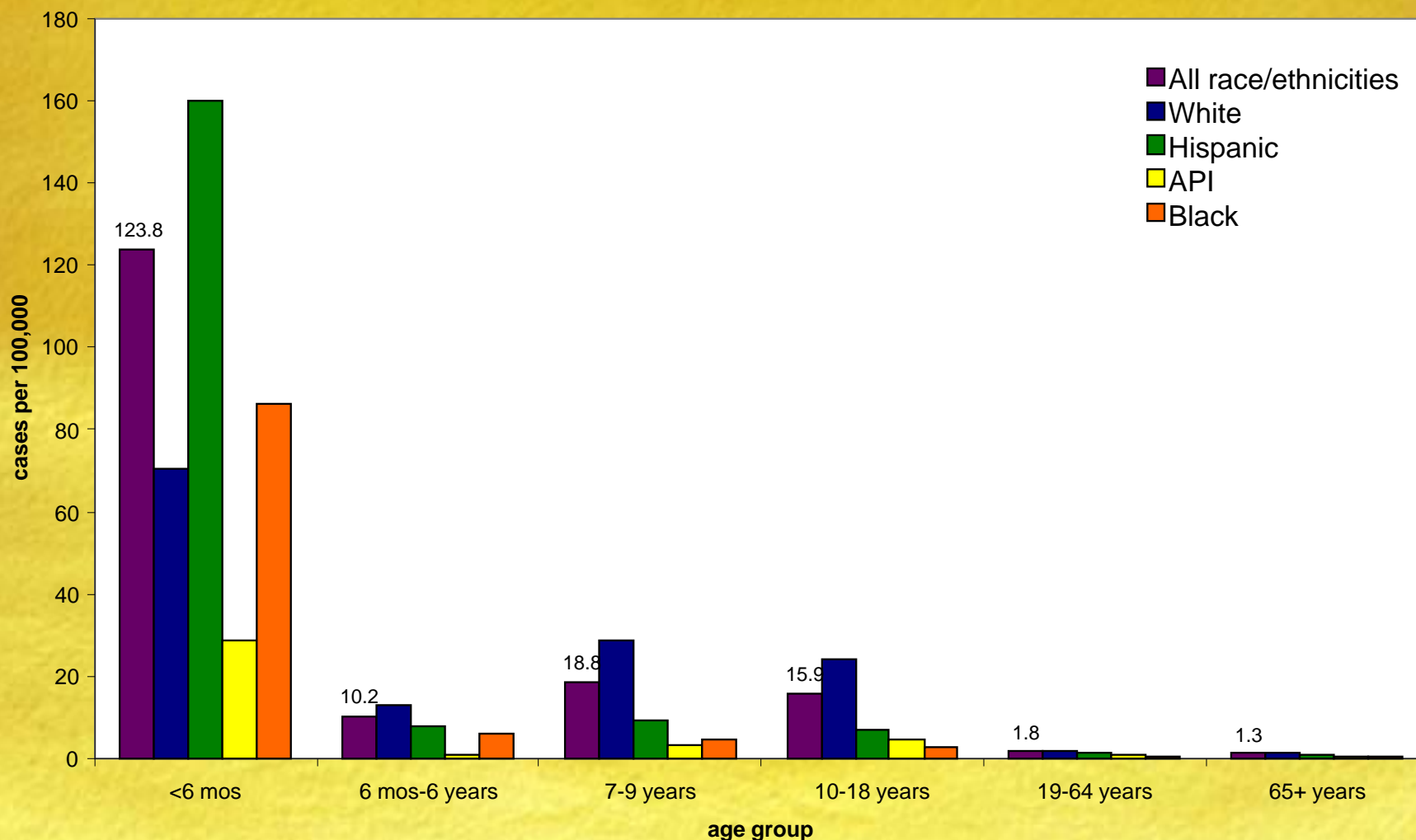


# Epidemic curve of pertussis cases California, 2005 & 2009-2010



\*As of 8/3/2010; data are incomplete due to reporting delays

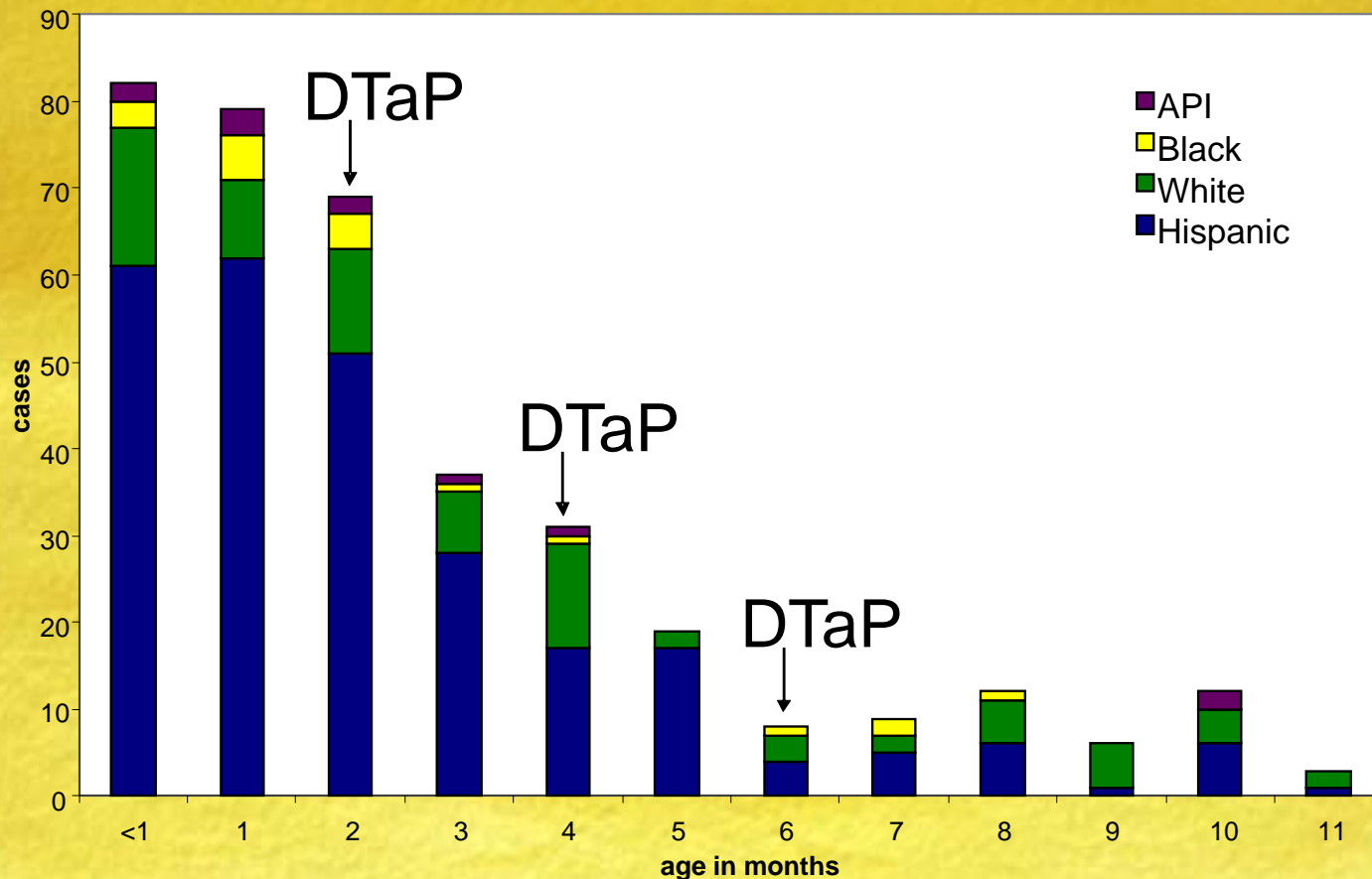
# Incidence of pertussis cases by race/ethnicity and age, California 2010



\*As of 8/3/2010



# Infant Pertussis Cases California 2010



\*As of 8/3/2010



# Clinical Presentation: Classic

- Incubation: 7-10 days (range: 5-21 days)
- Catarrhal (1-2 weeks)
  - ⊙ Nonspecific: runny nose, congestion, mild cough
  - ⊙ Indistinguishable from minor URI's
- Paroxysmal (2-6 weeks)
  - ⊙ Classic paroxysms with inspiratory whoop and post-tussive emesis (can be more frequent at night)
  - ⊙ Well-appearance between episodes
- Convalescent (2-6 weeks up to months)
  - ⊙ Decreased frequency and severity of coughing
  - ⊙ Subsequent URI may reactivate cough





# Clinical Presentation: Atypical

- Young infants

- ⊙ May lack classic cough and whoop
- ⊙ May present with only apnea, bradycardia, or cyanosis without cough

- Adolescents/adults

- ⊙ May lack distinct stages and cough often milder (many report “choking” sensation)
- ⊙ May only manifest prolonged cough (>3-4 weeks)
- ⊙ 13-32% of adults/adolescents with cough >5 days have serologic evidence of pertussis

# Pertussis Pretenders

## ● Viral

- ⊙ RSV
- ⊙ Adenovirus
- ⊙ Parainfluenza virus

## ● Bacterial

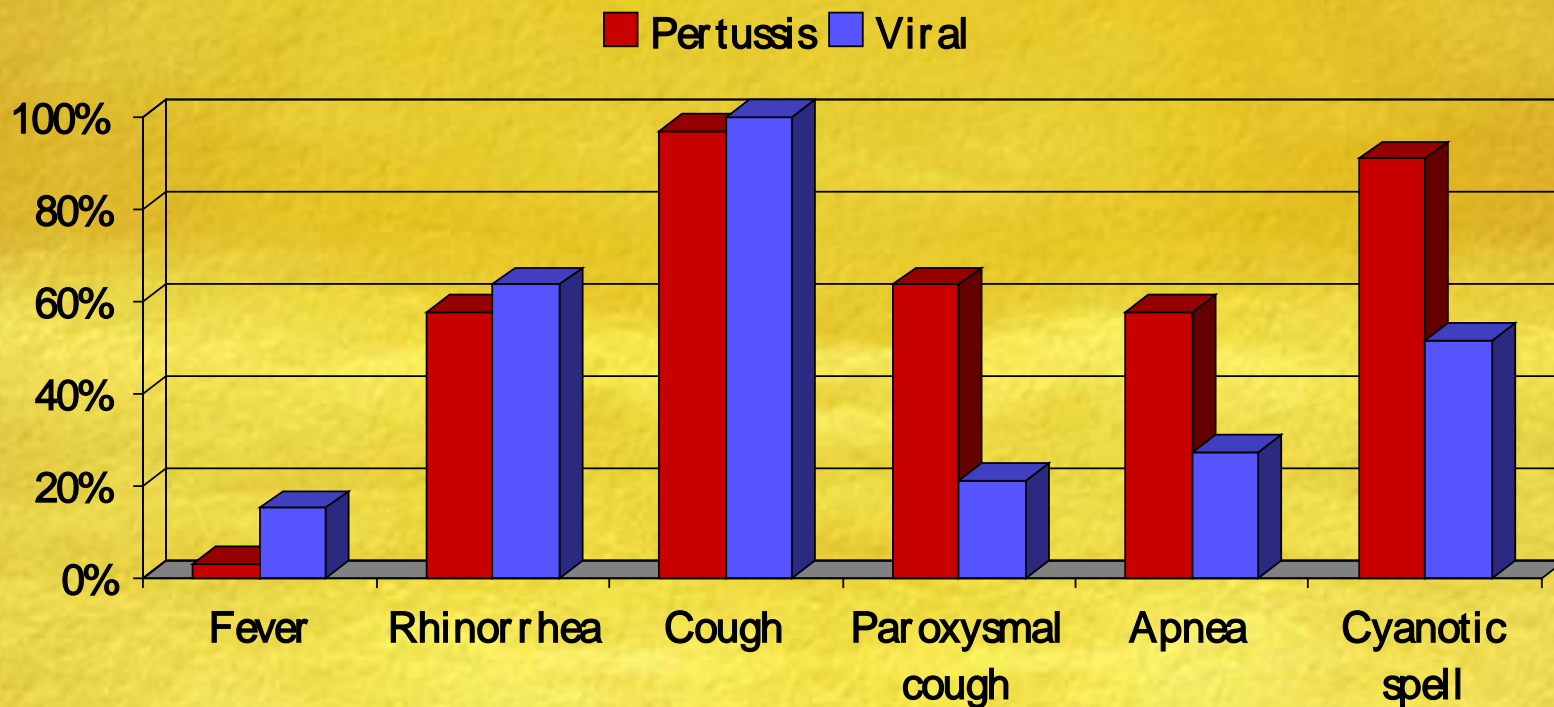
- ⊙ *Mycoplasma pneumoniae*
- ⊙ *Chlamydia trachomatis* and *pneumoniae*

## ● BEWARE: pertussis coinfection reported with several viruses:

- ⊙ RSV (0.6-8%)
- ⊙ Influenza
- ⊙ Parainfluenza
- ⊙ Adenovirus




# Clinical Characteristics of Pertussis in Infants $\leq 30$ days



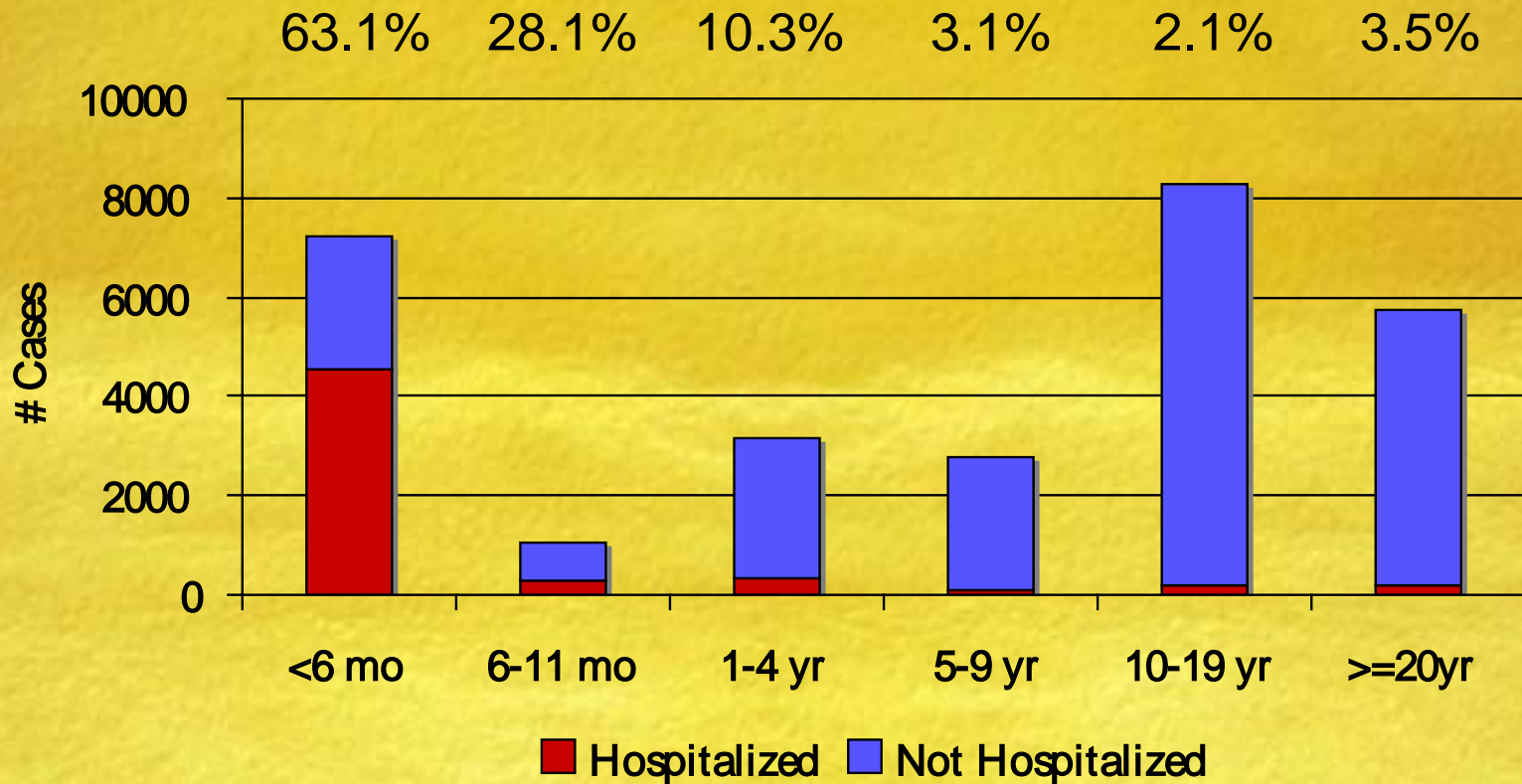


# Complications

- Infants/children: pneumonia, seizures, encephalopathy, death (often due to intractable pulmonary hypertension)
  - Adults/adolescents: pneumothorax, epistaxis, subconjunctival hemorrhage, subdural hematoma, hernia, rectal prolapse, urinary incontinence, rib fractures
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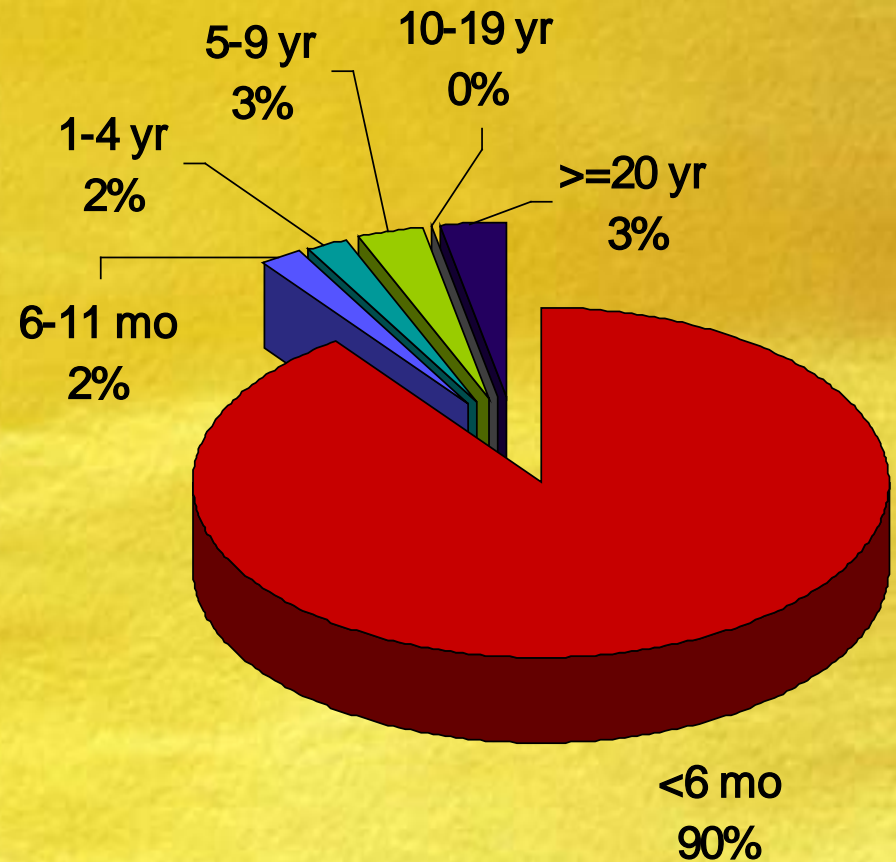


# Pertussis Hospitalizations



# Pertussis Mortality

- Death from pertussis occurs rarely but young infants <6 months of age are most at risk
- Risk factors for mortality
  - Female sex
  - BW <2500 grams
  - Apgar <8
  - Mother with <12 years of education
  - Hispanic infant <2 mos old (2.6x higher mortality)







# Pertussis Deaths in California

- Of the 7 deaths in 2010, all were Hispanic infants <2 mos (none had received any doses of DTaP)
- All pertussis deaths in CA since 1996, except one, have been in infants <3 months of age
- 80% Hispanic (compared with 50% birth cohort)
- Mean WBC in fatal cases from 1998-2009 was 75,000
- Of those with known status, all had pulmonary hypertension (extreme leukocyte mass obstructs pulmonary blood flow)

# Laboratory Testing

- WBC (helpful but nonspecific)
  - ⊙ WBC  $\geq 20K$  with  $\geq 50\%$  lymphocytes
  - ⊙ Absolute lymphocytosis  $\geq 10,000$  cells/uL
  - ⊙ Less often found in adults, adolescents, and immunized children



# Laboratory Testing

## ● NP culture - gold standard



- ◎ 100% specific, but sensitivity only 30-60%
  - ◎ Lower with previous vaccination or after antimicrobial treatment
  - ◎ Lower after  $\geq 2$ -3 weeks of illness
  - ◎ Higher with NP aspirate compared with swab
  - ◎ Higher with direct plating vs. using Regan Lowe transport media (charcoal)
- ◎ Growth takes 3-4 days (incubate culture plates for at least 7 days; 10 days recommended by CDPH)

CDC. *Guidelines for the Control of Pertussis Outbreaks*, 2000.  
CDC. *MMWR* Dec 15, 2006;55:RR-17.  
CDPH. Pertussis: Laboratory Testing, March 2010.

# Laboratory Testing

- *B. pertussis* PCR (NP aspirate or swab)
  - ⊙ Rapid with high sensitivity but lower specificity
  - ⊙ No standardized PCR protocol (variation in DNA purification, primers, probes, and QA)
  - ⊙ Many amplify single target (IS481) which cross reacts with *B. holmesii* and *B. bronchiseptica* (kennel cough) which uncommonly cause disease in humans
  - ⊙ False positive PCR's have resulted in unnecessary and resource-intensive control measures






# Healthcare worker with “Pertussis”

- Pediatric ED triage nurse presented to EH with 2-week h/o cough “just like the cough of the children I’ve seen with pertussis”
- No known exposure, no h/o Tdap
- NP swab POS by *B. pertussis* PCR
- Nurse furloughed and started on 5-day course of azithromycin



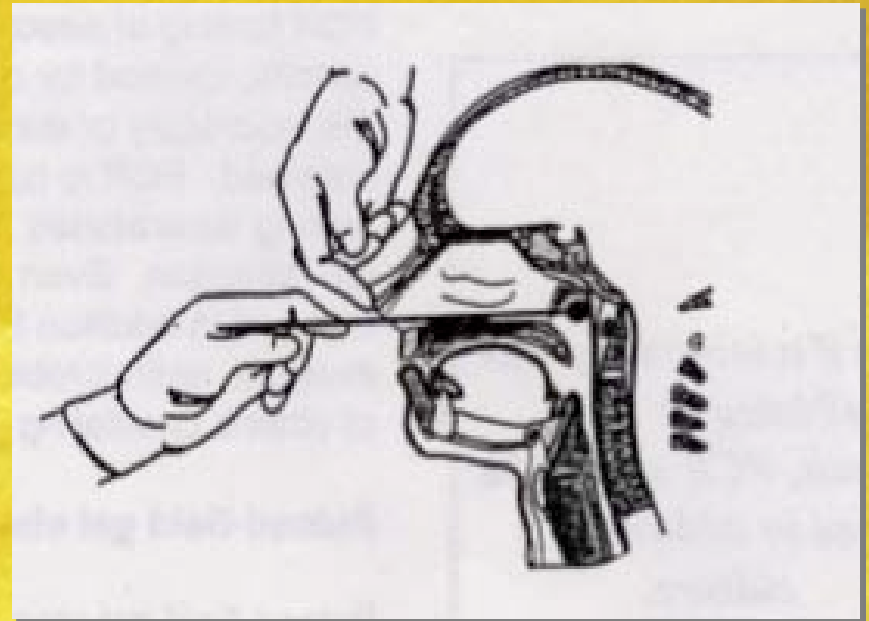
# Healthcare worker with “Pertussis”

- Contact investigation and prophylaxis
    - ⊙ 25 pediatric patients and their caregivers
    - ⊙ 26 staff members
    - ⊙ 15 attendees at educational conference
  - Due to epidemiologic implications, DNA sequenced and confirmed *B. holmesii*
- 



# Specimen Collection: Tips

- For NP swab, use Dacron (not cotton or Ca alginate) & leave in posterior NP for 10 secs
- For culture, place swab in charcoal transport media or inoculate plate
- For PCR, place swab in UTM (pink)
- Transport to lab promptly





# Other Laboratory Tests...

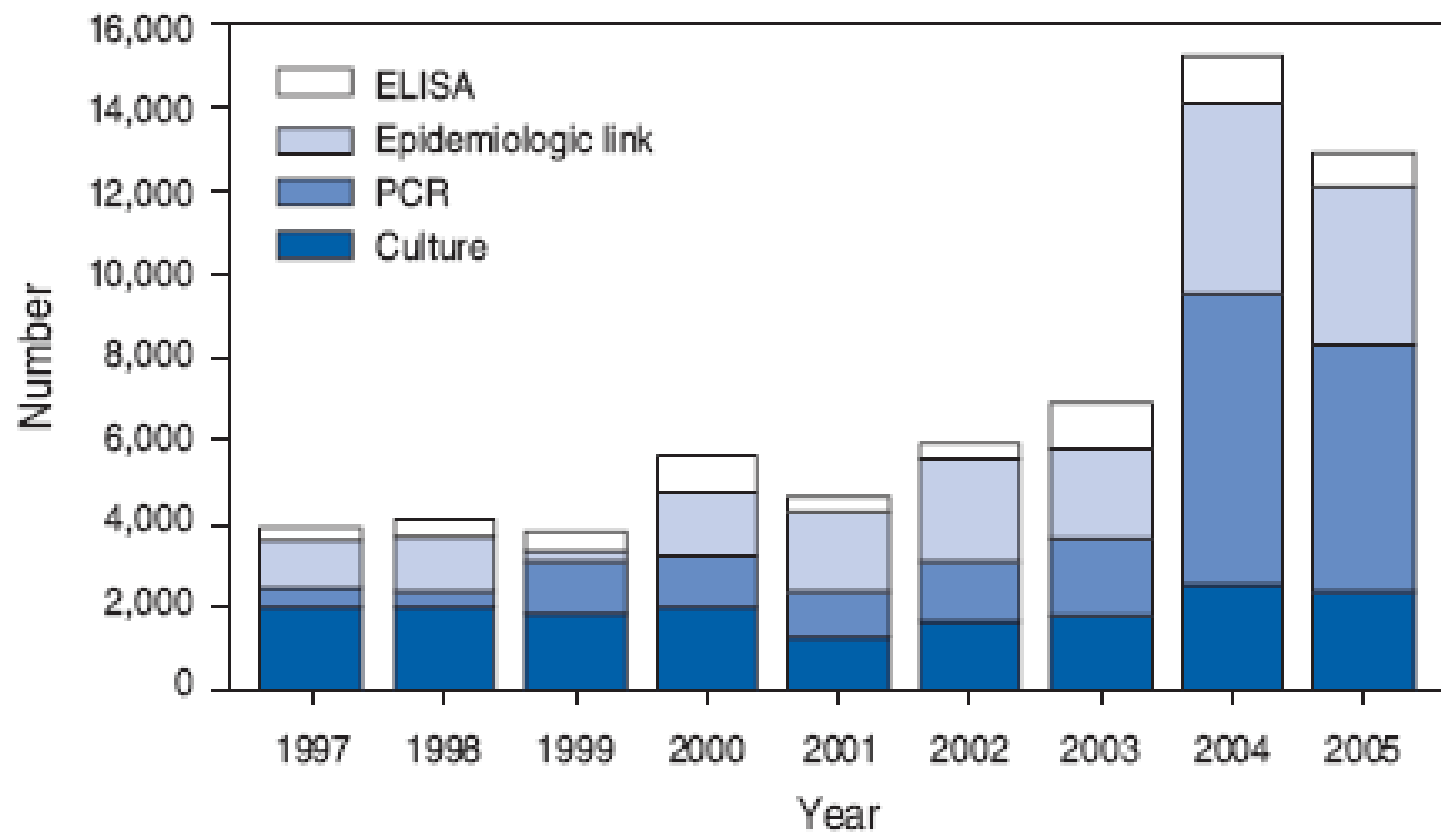
- NP DFA (not recommended)
  - ⊙ Sensitivity only 10-50%
  - ⊙ Specificity limited because test interpretation is subjective and cross reactions with normal flora in up to 85%
- Serology (not useful for immediate diagnosis)
  - ⊙ Acute & convalescent phase sera at least 4-weeks apart
  - ⊙ Single-sample serology for PT IgG collected after 3 weeks of symptoms if >2 years from last pertussis-containing vaccine



# Diagnosis

- Optimally, obtain NP culture and NP PCR (if <3 weeks of cough)
  - ⊙ Culture: media not readily available in office setting, low yield, delay
  - ⊙ PCR: difficulty obtaining optimal specimen, false positives, delay
- Ultimately, pertussis is a clinical diagnosis

# Number of Confirmed Pertussis Cases by Confirmation Method





# Treatment

- Primary role of treatment is to hasten clearance of organisms and limit transmission
  - ⊙ Treat as late as 3 weeks after cough onset if age >1 year
  - ⊙ Treat as late as 6 weeks after cough onset if age <1 year
- Treatment during catarrhal or early paroxysmal stage *may* modify duration and severity of illness
- Otherwise treatment generally does not affect clinical course

CDC. *MMWR* 2005;54:RR-14.

Altunaiji S et al. *Cochrane Reviews* 2007, Issue 3.



# Prophylaxis

- If within 3 weeks of exposure, prophylaxis recommended for all household and close contacts (regardless of age or vaccination status)
- If 3 weeks have elapsed since exposure, still consider prophylaxis for households with high risk contacts:
  - Young infants
  - Pregnant women
  - People who have contact with young infants





# Regimens for Treatment/Prophylaxis

- Primary agents: macrolides
  - ⊙ Erythromycin x 14 days (risk: IHPS in <1 mos)
  - ⊙ Clarithromycin x 7 days
  - ⊙ **Azithromycin x 5 days**
    - ⊙ Infants <6 mos: 10 mg/kg daily for 5 days
    - ⊙ Infants ≥6 mos and children: 10 mg/kg on day 1 (max: 500 mg), followed by 5 mg/kg daily on days 2-5 (max: 250 mg)
- Alternate agent: TMP/SMX x 14 days (age ≥2 mos)
  - ⊙ If patient unable to tolerate macrolides
  - ⊙ If pertussis isolate is macrolide-resistant (rare)




# Does anything help the clinical course?

- Studies have evaluated several therapies
  - ⊙ Antihistamines (diphenhydramine)
  - ⊙ Pertussis immunoglobulin
  - ⊙ Corticosteroids (dexamethasone)
  - ⊙ Beta-2 agonists (salbutamol)
- Current evidence (poor quality) does not demonstrate clinical benefit with these agents





# Critically Ill Patients with Pertussis

- Given risk of severe disease, low threshold for admitting young infants (especially <3 months of age) with pertussis
  - Patients that develop pneumonia with refractory hypoxemia, pulmonary hypertension, and cardiac failure
    - Double volume exchange transfusion
    - ECMO (mortality approaches of 70%)
- 




# Precautions

- Hospital/outpatient clinics

- Droplet precautions (i.e. wear surgical mask) for any patient with suspected pertussis
- Continue precautions for 5 days after initiation of effective therapy

- Child care/school

- Symptomatic children excluded until completion of 5 days of effective therapy
  - If not treated, exclude for 21 days from cough onset
- 






# Prevention: Vaccination

## DTaP

- Infants & children <7 years of age
- 3-dose efficacy: 59-89%
- Major problems:
  - ⊙ Least effective of childhood vaccines
  - ⊙ Does not fully protect those most at risk

## Tdap

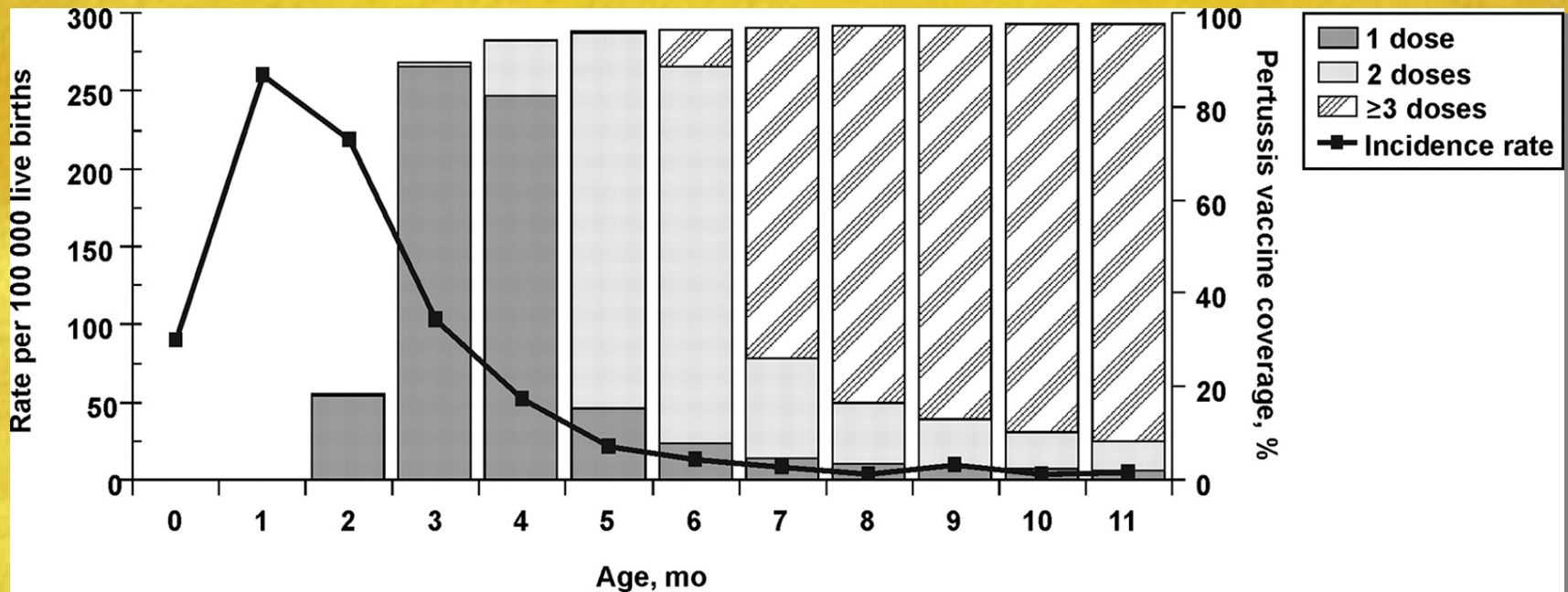
- Adolescents/adults in place of one Td
    - ⊙ ADACEL: 11-64 years
    - ⊙ BOOSTRIX: 10-18 years
  - FDA-approval based on immunogenicity, not efficacy
  - Major goal to reduce reservoir of infection for young infants
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# CDPH Pertussis Vaccination Recommendations

- Accelerate infant vaccination schedule
  - ⊙ Give first DTaP at 6 weeks
  - ⊙ Give doses 2 and 3 at intervals of 4 weeks (AAP)
- Even one dose has been associated with:
  - ⊙ Prevention of hospitalization (68% effective)
  - ⊙ Reduction in risk of severe disease (ICU care, mechanical ventilation, death)



# Incidence of pertussis hospitalization and vaccine coverage



# CDPH Pertussis Vaccination Recommendations

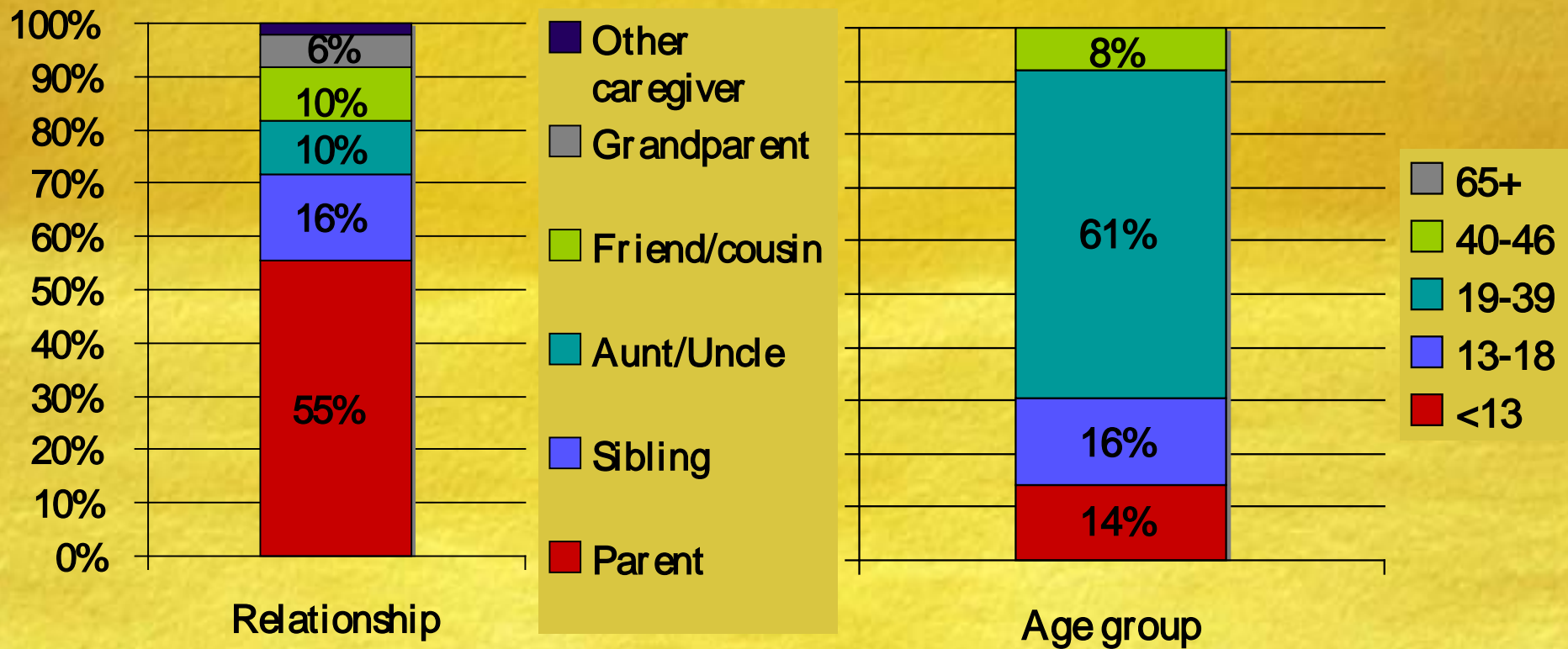
- Immunize priority populations with Tdap (“cocooning”) (assuming no prior receipt)
  - ⊙ Women of childbearing age
    - ⊙ Preferably before pregnancy
    - ⊙ Otherwise during pregnancy in 2nd or 3rd trimester or postpartum (prior to hospital/birthing center discharge)
  - ⊙ Other close contacts including:
    - ⊙ Parents and caregivers (even those  $\geq 65$  years of age)
    - ⊙ Children/adolescents  $\geq 10$  years of age
  - ⊙ Healthcare personnel (required by Cal/OSHA)
  - ⊙ Patients with wounds (Tdap instead of Td in patients  $\geq 7$  years )

CDC. *MMWR* May 30, 2008;57:RR-4.

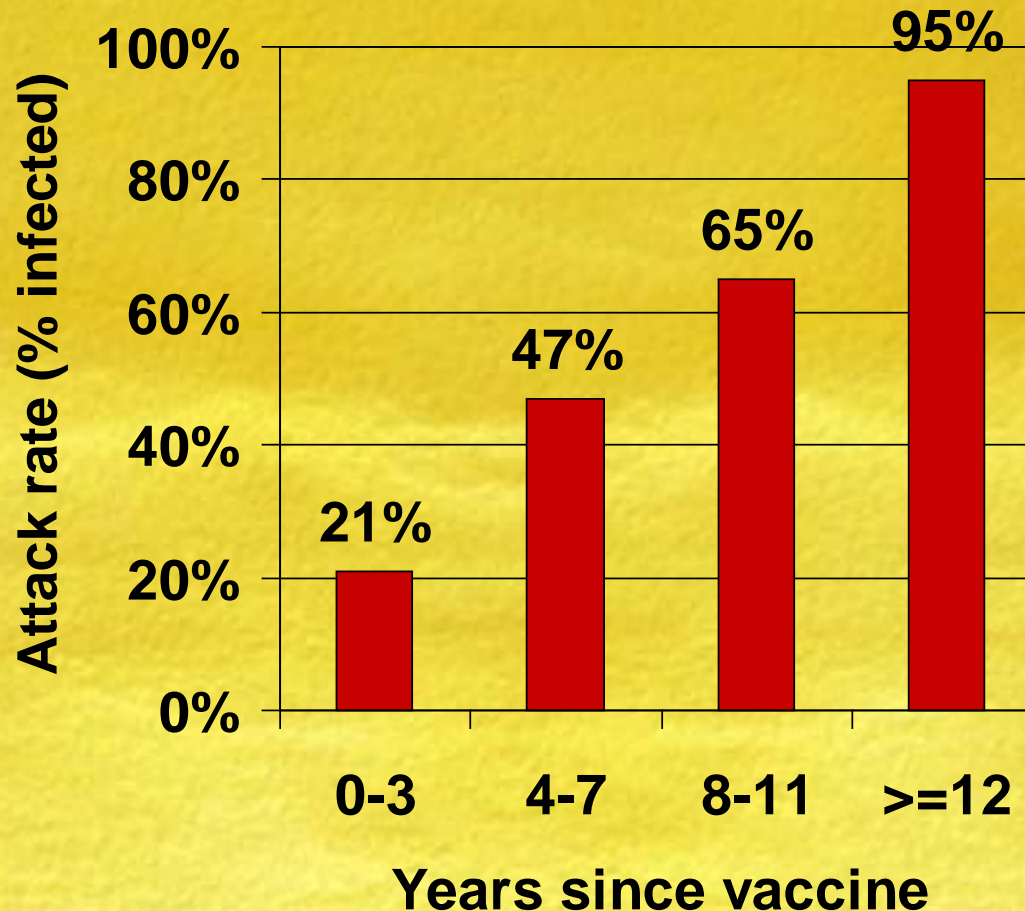
CDPH. Pertussis Vaccination Recommendations, 2010.



# Source of pertussis for infants is often a parent...



# Protection from vaccination wanes over time



Edwards KM. *PIDJ* 2005;24:S104-S108.

Cherry JD, *Pediatrics* 2005;115:1422-27.




# **Tdap vaccination coverage: Much room for improvement**

- 2007: 2.1% of adults nationally (18-64 years) reported receiving Tdap in prior 2 years
- 2008: 40.8% of adolescents (13-17 years) got Tdap in U.S.
  - ⊙ 41.9% for Hispanics
  - ⊙ 43.7% in California


# CDPH Pertussis Vaccination Recommendations

- No minimum interval between Td and Tdap
- Expanded ages for Tdap vaccination (off-label use permitted by law)
  - ⊙ Children  $\geq 7$  years: Tdap recommended for any child  $\geq 7$  years with incomplete DTaP series
  - ⊙ Adults  $\geq 65$  years
- Only absolute contraindications for Tdap
  - ⊙ H/o anaphylaxis to Tdap or DTaP
  - ⊙ Encephalopathy within 7 days of pertussis immunization (not due to another cause)

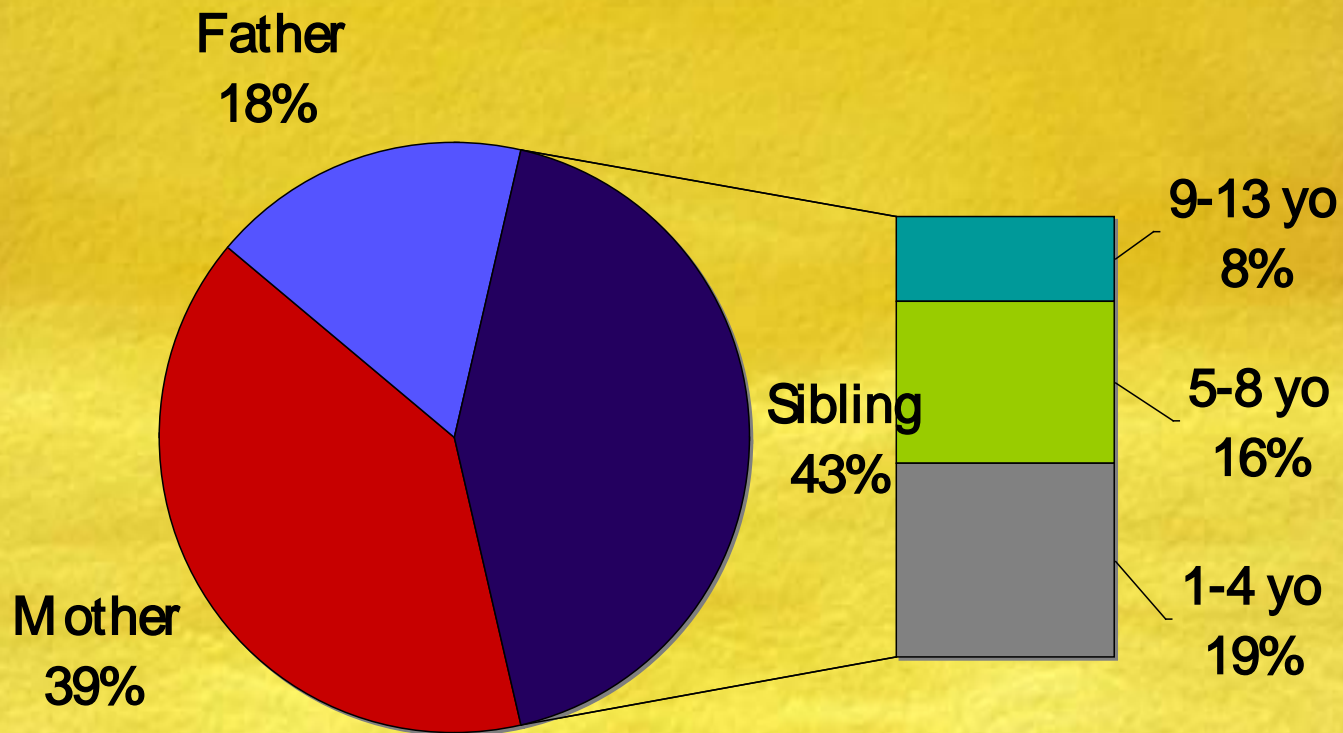




# Further Strategies to Complete “Cocoon”

- Ensure that all children are up to date on their DTaP vaccinations
  - For close contacts of young infants, consider:
    - ⦿ DTaP at 12 months of age (as long as at least 6 months since last dose)
    - ⦿ DTaP at age 4 years of age
- 

# Source of pertussis for infants can be a sibling...





# Which is pertussis?


- 1) 23-do girl with respiratory distress, apnea & bradycardia, progressing to respiratory failure and death, despite erythromycin (NP DFA + for Influenza A)
- 2) 2-mo with paroxysmal cough, worsening despite 2-weeks of erythromycin (NP DFA and culture negative for pertussis on admit)
- 3) 3-yo with recurrent paroxysmal cough and inspiratory stridor associated with fevers and pneumonias over 4 months, despite erythromycin (pertussis FHA IgM positive)



# Case #1: YES!

- Right age (for hospitalization, severe disease, and mortality)
- Right symptoms (apnea, cyanosis, bradycardia)
- WBC elevated with mostly lymphocytes
- Coinfection with other viral pathogens has been reported
- Erythromycin may not change clinical course

**Two days after death, NP culture from admission turned positive for *B. pertussis***





## Case #2: YES!

- Right age (for hospitalization, severe disease)
- Right symptoms (paroxysmal cough)
- WBC elevated with mostly lymphocytes

Repeat NP culture positive for *B. pertussis*

- *B. pertussis* resistant to erythromycin
- Patient treated with TMP/SMX and recovered

## Case #3: NO!

- Less common for children this age to develop severe pertussis requiring hospitalization
- High fevers and severe exacerbations over several months unusual for pertussis
- WBC elevated but with mostly neutrophils
- FHA antibodies may be caused by non-pertussis *Bordetella* and other infectious agents (only PT is specific to pertussis)

**Patient underwent bronchoscopy and found to have sunflower seed in trachea**



# Thank you for coming!



Please get your Tdap before this happens to you!